cases I now recommend it. In addition to its usefulness in enteroptosis it is valuable after abdominal sections, and especially after drainage cases, in which I ordinarily have used the binder, this corset accomplishes the work much more satisfactorily. The abdominal binder has to be held down by perineal straps, making it very disagreeable in the summer time; while the corset is held down by the garters with much less discomfort.

DR. A. ERNEST GALLANT, New York: The photographs show that with this corset properly adjusted the stomach is in the right position. With my corset the patient would have a straight line to the top of the corset. The thickness of the padding inside the corset is a matter of taste and necessity. If the woman is very thin we make it thick. I always try to secure a graceful figure. If the woman is ten pounds under weight more padding is put in. The special point is to pad enough and to place the padding just behind the anterior superior spine to relieve pressure. Every corset-maker should endeavor to make the corset a work of art as well as scientifically useful.

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# PHAGOCYTIC IMMUNITY AND THE THERAPEUTIC INJECTION OF DEAD BACTERIA IN ENDOCARDITIS.

## A PRELIMINARY REPORT.*

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### INTRODUCTION.

Our knowledge of the factors which determine the localization of micro-organisms on the endocardium in endocarditis, their maintenance and the means of defense on the part of the host is still obscure.

It is not difficult to understand how the endocardium becomes involved during lobar pneumonia with its pneumococcemia or in septicopyemic conditions due to the streptococcus or staphylococcus. In fact, in these cases this is what we would occasionally expect. The cases of endocarditis, on the other hand, that develop insidiously from no demonstrable source of infection or from an infection which is slight and which run a more chronic and milder course are more difficult to understand.

In fourteen cases of pneumococcus endocarditis of the latter type the pneumococci isolated from the blood before and after death were readily taken up *in vitro* by leucocytes in the patient's normal blood. They possessed no virulence, or very slight, to animals. This observation was made also in a case of staphylococcus endocarditis.

The pneumococci isolated from the blood in lobar penumonia, on the other hand, uniformly resist phagocytosis and possess a correspondingly high grade of virulence to animals.[1]

How do the micro-organisms in endocarditis of this mild type protect themselves in the blood and endocardium and ultimately cause death when they seem to be without virulence, while those in pneumonia with their high grade of virulence are usually destroyed and recovery is the rule? The object of this study was primarily to explain, if possible, the mechanism involved in these and other allied questions and to determine the effect of the therapeutic injections of dead bacteria in endocarditis. A full report of the experiments will appear later.

### CONSIDERATION OF CASES.

Clinically the cases are all characterized by a subacute course, and, while they must be regarded as cases of malignant endocarditis in that the patients all succumbed to the infection, they should properly be classed under the group designated in Osler's recent communication as chronic septic endocarditis. All but three occurred in patients between 15 and 29 years of age. The occupation of all was chiefly in doors. Six of each sex were affected. In nine cases the original source of infection could not be determined; in one it seemed to be an attack of tonsillitis; in another the most probable source was pyorrhea alveolaris; while in still another it was an abscess of the alveolus and tooth. The exact duration of the process could not be accurately determined but probably ranged from four to twelve months or more in the different cases. The blood culture was the means of making an early positive diagnosis in almost all of the cases. The making of a correct diagnosis on the clinical grounds in most of the cases was difficult because of the insidious onset, the chronicity, and, most of all, because the acute process was engrafted on an old valvular lesion in seven cases. In three cases this point could not be definitely settled, while in four no definite heart lesion was present. Of the four last mentioned there was a definite source of infection in two, while in the other two there was none. Petechial hemorrhages in the skin, one of the much sought-for signs in endocarditis, occurred late in nearly every one of the cases, long after the blood showed pneumococci. Probably the most constant feature was the development of an anemia of a secondary type. This was most pronounced in the cases which ran a more chronic course. A persistent leucocytosis was present in only four of the cases; the rest showed little or only temporary increase in the number of leucocytes. The leucocytosis was excessively high in the case of peculiar staphylococcus endocarditis, going to 120,000 just before death. Definite chills occurred only rarely and in no case in which chills seemed to mark the onset of the disease. Early the fever was remittent in type. In some patients the temperature was normal for weeks and then showed an afternoon rise for a short period. Later as embolism and petechial hemorrhage occurred the fever took on a septic or intermittent type and was associated with sweats.

Autopsies were obtained in six of the cases. Anatomically the valvular lesions were all characterized by huge vegetative growths on the valves involved. Usually the surfaces of the vegetations were studied with recent small necrotic areas and ulcers. The infarcts found showed no suppuration.

### BLOOD CULTURES.

It is an accepted fact that fluid media are more efficacious than solid media in routine blood cultures. All observers have obtained a higher percentage of positive results by this means in pneumonia, typhoid fever and septic processes generally. In endocarditis of the type under consideration, on the other hand, solid agar media have given positive results repeatedly where the cultures in broth and milk remained sterile. For this and for the reason that the latter method is a means of obtaining a knowledge of the number of bacteria circulating in the blood, the importance of making inoculations in both liquid and solid media in all cases in which endocarditis is suspected may be emphasized. Repeated cultures in a number of cases showed that while the bacteriemia is constant, the number of bacteria is never

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*I wish to express my gratitude, especially to Dr. Billings, in whose service all but three of the cases occurred; to Drs. Sippy, Herrick and C. T. Clark, for one case each, and to Dr. Hektoen for aid in the work.

1. Human Pneumococcal Opsonins and the Antiopsonic substance in Virulent Pneumococci. Jour. Infect. Dis., 1907, p. 285.

very great. The number of colonies varied between 4 and 2,000 per c.c. of blood. The organisms isolated from the blood before and after death are undoubtedly pneumococci in all but one case, which yielded a staphylococcus with certain peculiarities. The pneumococci isolated are quite different from those isolated from the blood in lobar pneumonia. As above stated, they are freely susceptible to phagocytosis when isolated and possess practically no virulence to animals. They grow tightly to the surface of the blood agar and in clumps of broth and in the fibrin clot of the blood culture in broth. The properties were more pronounced in some strains than others, and in one case became more pronounced as time went on. These properties are lost sooner or later on artificial cultivation and on animal inoculations, the organisms then taking on the characteristics of typical pneumococci.

### ANIMAL EXPERIMENTS.

The characteristics just mentioned are believed to be environmental modifications and to bear a close relation to the ability of the organisms to produce endocarditis. By inoculations into animals of hugh doses of the organisms before the special characteristics were lost, endocarditis resulted without injury of the valves in case of all of the strains tested (six), endocarditis being produced in sixteen rabbits without injury of the valves. Pericarditis developed in every instance in which the endocardium was involved. This was quite independent of the place of inoculation. The special affinity these organisms had for the endocardium, pericardium and the intima of the blood vessels is striking. Intraperitoneal and usually subcutaneous injections as well cause no lesions in these regions but produce a pericarditis and endocarditis instead, especially when a simultaneous dose is injected intravenously. In order to produce endocarditis it was necessary to inject hugh doses and preferably into different regions of the body. The animals recovered promptly from the immediate effects of the injection. Blood and peritoneal cultures at the end of two or three days were sterile. Later, two or three weeks after the valvular lesion became pronounced, a loss of weight, fever and dyspnea occurred and in some instances a definite heart murmur developed.

After the special characteristics were lost it was no longer possible to produce endocarditis. The experimental production of endocarditis in the past has been considered quite impossible without trauma to the valves. The earlier attempts in this study were failures probably because the organisms were inoculated too long after isolation and injected in too small doses.

### THE OPSONIC INDEX AND THE THERAPEUTIC INJECTION OF DEAD BACTERIA.

Early the opsonic index is usually normal or a little above, depending on the presence or absence of extension or accidents, such as thrombosis and embolism. Toward the end it falls far below normal. Four cases showed a rise just before death. The injection of the homologous dead organisms early in these cases was followed in twenty-four and forty-eight hours by a rise in the opsonic index and in the leucocytes; usually there was also a corresponding rise in temperature. Clinically no change for the better or worse could be noticed so long as the index was up and the general condition of the patient good. Later, however, after the patient's condition was poor and the opsonic index far below normal, the rise in leucocytes and opsonic index was associated with a drop in the temperature and a definite improvement in the general condition. The rise in the opsonic index and in the number of leucocytes following the injection of dead bacteria is apparently not associated with the reduction in the bacteria circulating in the blood.

A painstaking study of the method by which the bacteria in these cases seemed to protect themselves against the antibodies of the host may be briefly summarized:

1. By cultivation in the serum and blood of the patient these organisms acquired a resistance to opsonification and phagocytosis instead of an increased susceptibility.
2. They usually grew more rapidly in the patient's serum than in normal serum.
3. While leucocytic normal blood had a marked bacteriolytic effect due to phagocytosis and intraleucocytic destruction, the patient's blood containing the same number of leucocytes, the serum having a high opsonic index, often had no bacteriolytic action. This seemed not wholly due to the lack of phagocytosis but to the inability of the leucocytes to destroy the bacteria after they had been taken up.

### CONCLUSIONS.

1. The blood culture in endocarditis is the best means of making an early diagnosis. It should always be made for the identification and study of the infecting organism as well as for prognostic reasons. Barring accidents, the greater the virulence the more grave the prognosis.
2. The therapeutic injection of dead bacteria in endocarditis has very little influence on the course of the disease until late in the course, when there is a temporary improvement following the injections.
3. A very close relation exists between the biologic character of these organisms and their ability to produce endocarditis in the class of cases observed.
4. The organisms isolated, while of practically no virulence to animals and susceptible to phagocytosis on cultivation, appear to immunize themselves against the antibodies produced by the host, and thus to overcome the resistance of the latter.

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## PRELIMINARY REPORT OF THE ANESTHESIA COMMISSION OF THE AMERICAN MEDICAL ASSOCIATION.*

At the session of this Section in Atlantic City, in 1906, the then Chairman, Dr. Bevan, made some interesting remarks on the value of nitrous oxid as a general anesthetic, and ventured to predict its more common adoption for major surgical procedures. So much interest was aroused by his statements, that this section resolved to appoint a commission to investigate broadly the subject of the numerous anesthetics, old and new, in order that, after proper deliberation, we might set forth an authoritative estimate of their proper value for the profession. In accordance with that resolution a commission was appointed, which has been engaged for some months on the prescribed problem.

Our task is far from simple. The ground to be covered is wide. The opinions of leading surgeons are often opposed and the anesthetics struggling for recognition are held in varying esteem by responsible persons of

* Read in the Section on Surgery and Anatomy of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.